

**REMARKS**

**I. 35 USC 102 Rejections**

A. The Office Action rejected claims 1-4, 6, and 8-10 under 35 USC 102(b) as being anticipated by US Pat. 5,292,362 (the '362 Patent). In particular, the Office Action asserted that the '362 Patent disclosed a composition in the form of liquid or gel comprising collagen and sugar such as fructose (the '362 Patent, col. 4, ll. 52-68; col. 5, ll. 9-28, 38-43) and the composition is activated through ultraviolet radiation (the '362 Patent, col. 5, ll. 56-60).

To the extent that the rejection may be applied to the amended claims, Applicants respectfully traverses.

The '362 Patent discloses a composition comprising a compound which include saccharide (the '362 Patent, col. 5, ll. 13-14). The '362 Patent further discloses that the saccharides "are preferably selected from oligosaccharides such as fructose, and polysaccharides such as cellulose compounds . . ." However, the '362 Patent does not disclose the claimed sugar material which is selected from the group consisting of glucose, ribose, threose, galactose, lactose, maltose, or any combination thereof. Therefore, the '362 Patent does not teach each and every element of the claimed invention.

Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

B. The Office Action rejected claims 1-4, 6, and 8-10 under 35 USC 102(b) as being anticipated by US Pat. 5,632,773 (the '773 Patent). In particular, the Office

Action asserted that the '773 Patent discloses a composition in the form of gel comprising collagen and sugar such as sucrose (the '773 Patent, col. 6, ll. 48-51; col. 7, ll. 21-30) and the composition is irradiated by ultraviolet or gamma radiation (the '773 Patent, col. 6, ll. 60-66).

To the extent that the rejection may be applied to the amended claims, Applicants respectfully traverses.

The '773 Patent states that "[e]xample of such additional components include oxygen-containing materials, such as sugars, starches, ketones and the like. Specific examples include sucrose, dextran and methyl vinyl ketone and the like." (The '773 Patent, col. 7, ll. 27-30). However, the '773 Patent does not disclose the claimed sugar material which is selected from the group consisting of glucose, ribose, threose, galactose, lactose, maltose, or any combination thereof. Therefore, the '773 Patent does not teach each and every element of the claimed invention.

Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

## **II. 35 U.S.C. 103 Rejections.**

The Office Action rejected claims 5 and 7 under 35 U.S.C. 103(a) as being unpatentable over any of the '362 Patent or the '773 Patent, each standing by itself, or in view of U.S. Pat. 5,716, 633 (the '633 Patent).

To the extent the rejections can be applied to the amended claims, Applicants respectfully traverse.

**A. The '362 Patent or the '773 Patent.**

The Office Action acknowledged that the '362 and '773 Patents do not teach gamma radiation subsequent to UV radiation. However, the Office Action was of opinion that it is within the skill in the art to select the polymerization technique depending on the desired character of the collagen based on the intended use because the nature of collagen is altered by the way of cross-linking. The Office Action asserted that "Applicants did not show superior or unexpected results from the exposure of the composition to gamma radiation subsequent to UV radiation." Accordingly, the Office Action concluded that the "exposure of the composition to gamma radiation subsequent to UV radiation does not render the claims patentable, absent evidence to the contrary."

At the onset, Applicants note that neither the '362 Patent nor the '773 Patent disclosed the claimed sugar materials which is selected from the group consisting of glucose, ribose, threose, galactose, lactose, maltose, or any combination thereof. The Office Action acknowledges that neither the '362 Patent nor the '773 Patent disclose the gamma radiation subsequent to UV radiation. Applicants are puzzled at how an ordinarily skilled artisan, upon the teaching in the '362 or '773 Patents, would arrive at the claimed invention of claims 5 and 7.

Prior to the present invention, it was well known that gamma irradiation denature collagen molecules by decreasing the molecule's strength and increasing its susceptibility to enzymatic degradation (The Specification, para. 0010, p. 6, ll. 12 – 14; para. 0031, p. 10, ll. 18 – 21). Therefore, the manufacturers of collagenous

biomaterials must either accept the damage inflicted by gamma sterilization or abandon the use of collagenous materials (Para. 0010, p. 6, ll. 15-17).

Applicants unexpectedly discovered that the incorporation of a sugar material (e.g., glucose) into collagen and UV irradiation results a film more cross-linked than films treated with either glucose or UV alone (para. 0052, p. 18, ll. 15-16) and therefore synergistically enhances UV-induced crosslinking to yield a material with greater durability (para. 0031, p. 11, ll. 1-2). Applicants further discovered that, while gamma irradiation on glucose incorporated collagen has detectable effect on the integrity and enzyme resistance of the film (para. 0090, p. 31, ll. 20-21; see also Fig. 6, compare the "9mM Gluc + Gamma" bar to the "9mM Gluc + UV" bar), the films produced by glucose incorporation and UV irradiation followed by gamma irradiation are not highly denatured (para. 0090, p. 31, l. 21, to p. 32, l. 1; see also, Fig. 6, compare the "9mM Gluc + UV" bar to the "9mM + UV + Gamma" bar and the "9mM Gluc + Gamma" bar). Therefore, gamma irradiation without prior exposure to UV highly denatures the material (Fig. 6, the "9mM Gluc + Gamma" bar), however, gamma irradiation subsequent to UV irradiation results much less denatured material (Fig. 6, the "9mM Gluc + UV + Gamma" bar). Accordingly, the incorporation of a sugar material (e.g., glucose) into the collagen materials exposed to UV maintains strength and lessens gamma-induced denaturing effects (Para. 0090, p. 32, ll. 1-3).

Accordingly, Applicants demonstrate unexpected results by the exposing the claimed composition to UV radiation first and then gamma radiation.

**B. The '362 Patent or the '773 Patent, in view of the '633 Patent**

The Office Action asserted that the '633 Patent teaches collagen hydrogel for promoting epithelial cell growth during healing process and the collagen hydrogel is exposed to gamma radiation and then placed under UV light (the '633 Patent, col. 13, ll. 54-59). The Office Action concluded that it would have been obvious to one having ordinary skill in the art at the time of the invention to provide composition comprising irradiated sugar and collagen as disclosed by both the '362 Patent and the '773 Patent and perform both gamma and UV irradiation as disclosed by the '633 Patent, motivated by the teaching of the '633 Patent that the collagen hydrogel produced through cross-linking via irradiation promotes epithelial cell growth during healing process, with reasonable expectation of having an irradiated composition comprising sugar and collagen mixture that is used successfully in wound healing compositions.

Applicants note that the '633 Patent disclose a collagen-hydrogen material which is a hydrogen polymer formed by the free radical polymerization of a hydrophilic monomer solution gelled and crosslinked in the presence of an aqueous stock solution of collagen to form a three dimensional polymeric meshwork for anchoring collagen (The '633 Patent, the Abstract). The '633 Patent states:

The collagen-hydrogel of this invention differs from those known in the prior art because of the crosslinking of the hydrogel into a three dimension meshwork for anchoring macromolecules capable of supporting anchor-dependent cell growth. Generally hydrogels per se are formed by forming a cross-linked polymer in an aqueous solution to gel the solution. This can be done by free radical polymerization of hydrophilic monomers, such as hydroxyethylmethacrylate (HEMA).

The '633 Patent, col. 11, ll. 25-33.

Accordingly to the '633 Patent, the macromolecules include collagen (The '633 Patent, col. 11, ll. 39-41) and the hydrophilic monomer includes hydroxyethylmethacrylate (HEMA) (the '633 Patent, col. 11, ll. 31-32).

The '633 Patent further teaches that a collagen-hydrogel monomer solution is exposed to gamma radiation or UV radiation to polymerize the monomer solution and the resulting collagen-hydrogel is then placed under UV light for two hours (the '633 Patent, col. 12, ll. 54-60). Thus, the '633 Patent teaches UV irradiation subsequent to gamma irradiation to the collagen-hydrogel monomer solution

The '633 Patent, however, does not teach that the hydrophilic monomer is a sugar material. It does not teach or suggest that UV irradiation subsequent gamma irradiation can be applied to the composition of the '362 Patent and the '773 Patent, or the claimed composition in the present invention. In addition, although the '633 Patent teaches UV irradiation subsequent to gamma irradiation, it does not teach gamma irradiation subsequent UV irradiation.

As discussed in Sections (I)(A) & (B) of this response, neither the '362 Patent nor the '733 Patent disclosed the claimed sugar materials which is selected from the group consisting of glucose, ribose, threose, galactose, lactose, maltose, or any combination thereof, let alone the exposure to gamma radiation subsequent to UV irradiation.

To make a *prima facie* case of obviousness rejection, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference themselves or in the knowledge of ordinary skill in the art, to modify the reference or to

combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P 2143.

Applicants find no suggestion or motivation to combine the cited reference together. In particular, the fact that the collagen-hydrogel of the '633 Patent, produced by the disclosed irradiation process (UV irradiation subsequent to gamma irradiation), promotes epithelial cell growth during a healing process does not provide motivation to apply the irradiation process of the '633 Patent to the compositions in the '773 Patent or the '362 Patent, since the '633 Patent explicitly teaches that the "collagen-hydrogel of this invention differs from those known in the prior art because of the crosslinking of the hydrogel. . ." (The '633 Patent, col. 11, ll. 25-27).

By the same token, since the collagen-hydrogen of the '633 Patent differs from those known in the prior art, there is no reasonable expectation of success of applying the irradiation process (UV irradiation subsequent to gamma irradiation) of the '633 Patent to the compositions of the 773 Patent or the '362 Patent.

Even if the cited references were to be combined, the hypothetical combination would not have rendered all the limitations of the claimed invention, since neither the '362 Patent nor the '733 Patent teaches the claimed sugar material, nor does the '633 Patent teach gamma irradiation subsequent to US irradiation.

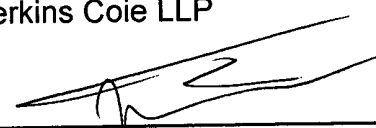
In light of the foregoing, Applicants respectfully request that the rejections to claims 5 and 7 be reconsidered and withdrawn.

**Conclusion**

In view of the foregoing, it is submitted that the present claims are in condition for allowance. Accordingly, a Notice of Allowance is respectfully requested.

Respectfully submitted,  
Perkins Coie LLP

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